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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,205	11/27/2000	Michael Kalchman	MC010PI	7948

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P O BOX 2000
RAHWAY, NJ 070650907

EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,205	KALCHMAN ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,13,14,16,17 and 20-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,13,14,16,17 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 November 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on September 18, 2003, applicant's response to the office communication filed on January 23, 2004, and applicant's response to Notice of Non-Compliant amendment filed on February 23, 2004 have been entered. The claims pending in this application are claims 7, 13, 14, 16, 17, and 20-25. Rejection and /or objection not reiterated from the previous office action are hereby withdrawn in view of the amendments. The following rejections are based on amendments.

Drawings

2. The examiner notes that applicant does not response to Notice of Draftsperson's Patent Drawing Review (PTO-948) mailed on June 3, 2003.

Specification

3. The substitute specification filed September 18 and January 23, 2004 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) since applicant does not submit a substitute specification in clean form without markings as to amended material.

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. The first page of WO 99/60986 in this instant application is not considered as a separate abstract sheet. Note that applicant does not address this issue (see previous office action mailed on June 18, 2003).

5. The use of the trademark "TRITON" has been noted in this application. For example, see page 16, lines 22 and 23. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Note that applicant does not address this issue (see previous office action mailed on June 18, 2003).

6. Following objections made in the office action mailed on June 18, 2003 are maintained since the substitute specification filed September 18, 2003 and January 23, 2004 has not been entered (see above)

The specification contains web sites. For example, in page 24, lines 13 of the specification, there is http://dot.imgen.bcm.tmc.edu:9331/seq.search/gene. search.html. Thus the disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The disclosure is objected to because of the following informality: (1) "a longer region of cDNA totaling 4795 bases" in lines 12 and 13 in page 5 should be "a longer region of cDNA totaling 4796 bases" since the length of HIP1 cDNA is 4796 bases (see SEQ ID NO: 3); and (2) in several places of the specification, applicant uses "C" to replace "^{0}C". For example, see page 15, last line.

Appropriate correction is required.

Claim Objections

7. Claim 7 is objected to because of the following informality: "encode" in line 3 should be "encodes".

8. Claims 13 and 14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. According to claim 7, the HIP apoptosis modulating protein is a HD-interacting polypeptide wherein said polypeptide consists of a sequence of amino acids selected from the group consisting of SEQ ID Nos: 2, 4, 5, and 7. Since the phrases "the HIP apoptosis modulating protein has a sequence as set forth in SEQ ID NO: 4" recited in claim 13 and "the HIP apoptosis modulating protein has a sequence as set forth in SEQ ID NO: 5" recited in claim 14 are read as "the HIP apoptosis modulating protein comprises a sequence as set forth in SEQ ID NO: 4" and "the HIP apoptosis modulating protein comprises a sequence as set forth in SEQ ID NO: 5", it appears that a sequence of the HIP apoptosis modulating protein (ie., comprising SEQ ID NO: 4 or 5) recited in claim 13 or 14 is equal or longer than a sequence of the HIP apoptosis modulating protein (ie., consisting of SEQ ID NO: 4 or 5) recited in claim 7. Therefore, claims 13 and 14 do not further limit claim 7. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

9. Claim 17 is objected to because of the following informality: delete "that" between "claim 16" and "is".

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 7, 14, 21, and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for encoding a HD-interacting polypeptide consisting of SEQ ID NO: 4 using an expression vector comprising an isolated nucleic acid molecule consisting of SEQ ID NO: 3, does not reasonably provide enablement for encoding a HD-interacting polypeptide consisting of a sequence of amino acids selected from the group consisting of SEQ ID Nos: 2, 5, and 7 using an expression vector comprising an isolated nucleic acid molecule consisting of SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Note that, since an expression vector comprising an isolated nucleic acid molecule consisting of SEQ ID NO: 3 can encode a HD-interacting polypeptide consisting of SEQ ID NO: 4, claims 13, 20, 22, 24, and 25 should not be included in the rejection below. Since a host cell comprising the expression vector of claim 7 comprising an isolated nucleic acid molecule consisting of a sequence of nucleotides as set forth in SEQ ID NO:3, claims 16 and 17 should not be included in the rejection below.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claim 7 is drawn to an expression vector comprising an isolated nucleic acid molecule consisting of SEQ ID NO: 3 that can encode a polypeptide selected from the group consisting of SEQ ID Nos: 2, 4, 5, and 7. Claim 14 indicates that SEQ ID NO: 3 can encode SEQ ID NO: 5. Claim 21 indicates that an isolated nucleic acid molecule consisting of SEQ ID NO: 3 that can encode a polypeptide consisting of SEQ ID NO: 5. Claim 23 is directed to a host cell transfected or transformed with an expression vector comprising the isolated nucleic acid molecule of claim 21. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001) (see below).

The Breadth of The Claims

Claim 7 encompasses an expression vector comprising an isolated nucleic acid molecule consisting of a sequence of nucleotides as set forth in SEQ ID NO: 3, which encodes an HD-interacting polypeptide, wherein HD-interacting polypeptide is a HIP-apoptosis modulating protein and wherein said polypeptide consists of a sequence of amino acids selected from the group consisting of SEQ ID NO: 2, 4, 5, and 7. Claim 14 encompasses an expression vector comprising an isolated nucleic acid molecule consisting of a sequence of nucleotides as set forth in SEQ ID NO: 3, which encodes a sequence comprising SEQ ID NO: 5. Claim 21 encompasses an isolated nucleic acid molecule consisting of SEQ ID NO: 3 that can encode a polypeptide

consisting of SEQ ID NO:5. Claim 23 encompasses a host cell transfected or transformed with an expression vector comprising the isolated nucleic acid molecule of claim 21.

Working Examples

The specification provides different working examples (see pages 11-31).

The Amount of Direction or Guidance Provided and The State of The Prior Art

The specification provides guidance to show that an isolated nucleic acid molecule consisting of SEQ ID NO: 3 can encode a HD-interacting polypeptide consisting of SEQ ID NO: 4 (see page 5, lines 3-14). However, there is no direction or guidance in the specification to show an isolated nucleic acid molecule consisting of SEQ ID NO: 3 can encode a HD-interacting polypeptide selected from the group consisting of SEQ ID NOs: 2, 5, and 7. In fact, sequence comparison among SEQ ID Nos: 2, 4, and 7 indicates that SEQ ID NO: 2 or SEQ ID NO: 7 is not part of SEQ ID NO: 4. Thus, an isolated nucleic acid molecule consisting of SEQ ID NO: 3 cannot encode a HD-interacting polypeptide selected from the group consisting of SEQ ID NOs: 2 and 7. Furthermore, although SEQ ID NO: 5 is longer than SEQ ID NO: 4 and has SEQ ID NO: 4 (see page 5, lines 3-14 and SEQ ID Nos: 4 and 5), the specification does not teach that an isolated nucleic acid molecule consisting of SEQ ID NO: 3 can encode SEQ ID NO: 5. Applicant does not provide an evidence to show that an isolated nucleic acid molecule consisting of SEQ ID NO: 3 can encode SEQ ID NO: 5 either.

Level of Skill in The Art, The Unpredictability of The Art, and The Quantity of Experimentation Necessary

While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether an isolated nucleic acid molecule consisting of

SEQ ID NO: 3 can encode a HD-interacting polypeptide selected from the group consisting of SEQ ID NOs: 2, 5, and 7. As mentioned previously, since the specification does not provide any guidance to show that an isolated nucleic acid molecule consisting of SEQ ID NO: 3 can encode a HD-interacting polypeptide selected from the group consisting of SEQ ID NOs: 2, 5, and 7, there will be a lot of unpredictable factors when the skilled artisan, based on claims 7, 14, and 21 of this instant application and the specification, uses an isolated nucleic acid molecule consisting of SEQ ID NO: 3 to encode a HD-interacting polypeptide selected from the group consisting of SEQ ID NOs: 2, 5, and 7. With the predictability in the relevant art being low, the amount of experimentation needed to be exerted by the public in practicing the full scope of the invention would not fall within the limits of routine experimentation. Such efforts constitute undue experimentation. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001 (see above). As set forth in the decision of the Court:

" '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
"Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
"It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement

requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether an isolated nucleic acid molecule consisting of SEQ ID NO: 3 can encode a HD-interacting polypeptide selected from the group consisting of SEQ ID NOs: 2, 5, and 7.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 7, 13, 16, 17, 20, 22, 24, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Kalchman *et al.*, (WO 97/18825, published on May 29, 1997).

The inventions are directed to an expression vector, a host cell, and an isolated nucleic acid molecule. Claim 7 requires that an expression vector for expression of a gene in a mammalian host comprising an isolated nucleic acid molecule consisting of a sequence of nucleotides as set forth in SEQ ID NO: 3, which encodes a HD-interacting polypeptide wherein the HD-interacting polypeptide is a HD apoptosis modulating protein and wherein said polypeptide consists of a sequence of amino acids selected from the group consisting of SEQ ID Nos. 2, 4, 5, and 7. Claim 13 requires that the HIP-apoptosis modulating protein has a sequence

as set forth in SEQ ID No. 4. Claim 16 requires that a host cell comprising the expression vector of claim 7. Claim 17 further limits claim 16 and requires that the host cell is a mammalian cell. Claim 20 requires an isolated nucleic acid molecule consisting of the nucleotide sequence as set forth SEQ ID NO:3. SEQ ID NOs:3 and 4 are HIP1 cDNA with 4796 nucleotides and its corresponding protein sequence with 914 amino acids (HIP1) respectively (see specification, lines 3-14 in page 5 and SEQ ID Nos: 3 and 4).

Kalchman *et al.*, teach protein which interacts with the Huntington's disease gene product, cDNA coding therefor, and antibodies thereto. The HIP1 cDNA sequence (SEQ ID NO: 5), which is 4796 nucleotide long, is translated into a polypeptide with 914 amino acids (see lines 3-8 in page 5 and SEQ ID Nos: 5 and 6 in page 25-31). Although it appeared that SEQ ID Nos: 5 and 6 had 4846 nucleotides and 924 amino acids respectively, in fact, there was mistakes in sequence numbers when Kalchman *et al.*, numbered SEQ ID Nos: 5 and 6 wherein nucleotides 3901-4796 in SEQ ID NO: 5 was numbered as nucleotide 3951-4846 and amino acids 751-914 was numbered as amino acids 761-924, the examiner has renumbered nucleotide and amino acid sequences in SEQ ID NO: 5 and SEQ ID NO: 6 respectively (see pages 25-31 in attached office action).

Regarding claims 7, 13, 20, and 22, comparison of nucleotide sequences between SEQ ID No: 5 in the reference of Kalchman *et al.*, and SEQ ID No: 3 recited in claims 7 and 20 and comparison of amino acid sequences between SEQ ID No: 6 in the reference of Kalchman *et al.*, and SEQ ID No: 4 recited in claims 13 and 22 show that SEQ ID NO: 5 in the reference of Kalchman *et al.*, is identical to SEQ ID No: 3 recited in claims 7 and 20 while SEQ ID NO: 6 in the reference of Kalchman *et al.*, is identical to SEQ ID No: 4 recited in claims 13 and 22. Since

an isolated nucleic acid molecule recited in claim 20 is read as an isolated nucleic acid molecule consisting of SEQ ID NO: 3 and SEQ ID NO: 5 in the reference of Kalchman *et al.*, is HIP1 cDNA with 4796 nucleotides and encodes a polypeptide with 914 amino acids (SEQ ID NO:6), claim 20 is anticipated by Kalchman *et al.*. Since SEQ ID NO: 3 encodes a polypeptide consisting of SEQ ID NO: 4 (see specification, lines 3-14 in page 5), claim 22 is anticipated by Kalchman *et al.*. Since Kalchman *et al.*, states that "because more of the expanded forms of the HD protein may be available for cleavage (and subsequent apoptosis) due to the fact they are not as tightly associated at the HD-HIP1-cytoskeletal complex" (see page 7, lines 5-10), HIP1 taught by Kalchman *et al.*, is a HD-interacting polypeptide or a HIP-apoptosis modulating protein as recited in claim 7. Since DNA encoding HIP 1 taught by Kalchman *et al.*, is cloned into an expression vector (see page 7, last paragraph) and an expression vector recited in claim 7 is read as an expression vector comprising an isolated nucleic acid consisting of SEQ ID NO: 3 which encodes a polypeptide consisting of SEQ ID NO: 4, claims 7, 13, and 25 are anticipated by Kalchman *et al.*.

Regarding claims 16, 17 and 24, since Kalchman *et al.*, teach DNA encoding HIP 1 (ie., consisting of SEQ ID NO:3) in an expression vector is introduced into a mammalian cell such as brain cells (see page 7, last paragraph) and the mammalian cell is a host cell, claims 16, 17, and 24 are anticipated by Kalchman *et al.*.

Kalchman *et al.*, teach all limitations recited in claims 7, 13, 16, 17, 20, 22, 24, and 25.

Response to Arguments

In page 5, fifth paragraph bridging to page 6, first paragraph of applicant's remarks filed on January 23, 2004, applicant argues that the amendments are sufficient to avoid anticipation by WO 97/18825.

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because SEQ ID NO: 5 in the reference of Kalchman *et al.*, is identical to SEQ ID No: 3 recited in claims 7 and 20 while SEQ ID NO: 6 in the reference of Kalchman *et al.*, is identical to SEQ ID No: 4 recited in claims 13 and 22 (for detail, see above rejection under 35 USC 102 (b)).

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. No claim is allowed.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
April 30, 2004

FRANK LU
PATENT EXAMINER

Thr Asp Thr Glu Ala Gly Cys Val Pro Leu Leu His Pro Glu Glu
1 5 10 15

Ile Lys Pro Gln Ser His Tyr Asn His Gly Tyr Gly Glu Pro Leu
20 25 30

Gly Arg Lys Thr His Ile Asp Asp Tyr Ser Thr Trp Asp Ile Val
35 40 45

Lys Ala Thr Gln Tyr Gly Ile Tyr Glu Arg Cys Arg Glu Leu Val
50 55 60

Glu Ala Gly Tyr Asp Val Arg Gln Pro Asp Lys Glu Asn Val Thr
65 70 75

Leu Leu His Trp Ala Ala Ile Asn Asn Arg Ile Asp Leu Val Lys
80 85 90

Tyr Tyr Ile Ser Lys Gly Ala Ile Val Asp Gln Leu Gly Gly Asp
95 100 105

Leu Asn Ser Thr Pro Leu His Trp Asp Thr Arg Gln Gly His Leu
110 115 120

Ser Met Val Val Gln Leu Met Lys Tyr Gly Ala Asp Pro Ser Leu
125 130 135

Ile Asp Gly Glu Gly Cys Ser Cys Ile His Leu Ala Ala Gln Phe
140 145 150

Gly His Thr Ser
154

(2) INFORMATION FOR SEQ ID NO:5:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4846
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: cDNA
(iii) HYPOTHETICAL: no
(iv) ANTI-SENSE: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: cDNA for Huntingtin-interacting protein
(xi)SEQUENCE DESCRIPTION: SEQ ID NO:5:

CAGTGTACGG TTGATCATAT AACGCCGCGG GCGGGGATTG GTTTATATAT 50
CGCAAATTGA TNTAGGGGGG GGGGGATGGN CAGAGATTTC GCTTCATTAG 100
GCCATTATAA GCAGGAAGGG TTTCAAGGAA AAAAACCCAG AAAGTGCATA 150
TTGCACCCAC CATGAGAAAG GGGCAACAGA CCTTNTGTTN TGTTNTCAAC 200

CGCCTGCTTC TGTTTTAGCA ACGCAGTGTT TTGGTGGAAG TTGTGCCATG 250
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CCTGCCTCCC AGCTGACACC CTGCAAGGCC ACCGGGACCG CTTCATGGAG 750
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CTTCAAGCGG CTCATTCAGA TCCCCCAGCT GCCTGAGAAC CCACCCAACT 850
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CCTCATGGAC ATGGATGCCT CTCAGCAGAA TTTATTTGAC AACAAGTTTG 1000
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CAAAATGGTG TGAACAAGGA TGAGAAGGAC CACTTAATTG AGCGACTATA 1100
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GATCTGGCCG AGCAGCAGCA CCTGCGGCAG CAGGCGGCCG ACGACTGTGA 1250
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TGGCCAGACA AGCCCAGGTA GATTTGGAAC GAGAGAAAAA AGAGCTGGAG 1500
GATTCGTTGG AGCGCATCAG TGACCAGGGC CAGCGGAAGA CTCAAGAACA 1550
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TCCAGCTGCA TCGAGCAACT GGAGAAAAGC TGGAGCCAGT ATCTGGCCTG 2000
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AACCCTCGCC TACCTGGCCT CCCTGGAGGA AGAGGGAAGC CTTGAGAATG 2200
CCGACAGCAC AGCCATGAGG AACTGCCTGA GCAAGATCAA GGCCATCGGC 2250
GAGGAGCTCC TGCCCAGGGG ACTGGACATC AAGCAGGAGG AGCTGGGGGA 2300
CCTGGTGGAC AAGGAGATGG CGGCCACTTC AGCTGCTATT GAAACTTGCA 2350
CGGCCAGAAT AGAGGAGATG CTCAGCAAAT CCCGAGCAGG AGACACAGGA 2400
GTCAAATTGG AGGTGAATGA AAGGATCCTT CGTTGCTGTA CCAGCCTCAT 2450
GCAAGCTATT CAGGTGCTCA TCGTGGCCTC TAAGGACCTC CAGAGAGAGA 2500
TTGTGGAGAG CGGCAGGGGT ACAGCATCCC CTAAAGAGTT TTATGCCAAG 2550
AACTCTCGAT GGACAGAAGG ACTTATCTCA GCCTCCAAGG CTGTGGGCTG 2600
GGGAGCCACT GTCATGGTGG ATGCAGCTGA TCTGGTGGTA CAAGGCAGAG 2650
GGAAATTTGA GGAGCTAATG GTGTGTTCTC ATGAAATTGC TGCTAGCACA 2700
GCCCAGCTTG TGGCTGCATC CAAGGTGAAA GCTGATAAGG ACAGCCCCAA 2750
CCTAGCCCAG CTGCAGCAGG CCTCTCGGGG AGTGAACCAG GCCACTGCCG 2800
GCGTTGTGGC CTCAACCATT TCCGGCAAAT CACAGATCGA AGAGACAGAC 2850
AACATGGACT TCTCAAGCAT GACGCTGACA CAGATCAAAC GCCAAGAGAT 2900

GGATTCTCAG GTTAGGGTGC TAGAGCTAGA AAATGAATTG CAGAAGGAGC 2950
GTCAAAAACT GGGAGAGCTT CGGAAAAAGC ACTACGAGCT TGCTGGTGTT 3000
GCTGAGGGCT GGGAAGAAGG AACAGAGGCA TCTCCACCTA CACTGCAAGA 3050
AGTGGTAACC GAAAAAGAAT AGAGCCAAAC CAACACCCCA TATGTCAGTG 3100
TAAATCCTTG TTACCTATCT CGTGTGTGTT ATTTCCCCAG CCACAGGCCA 3150
AATCCTTGGA GTCCCAGGGG CAGCCACACC ACTGCCATTA CCCAGTGCCG 3200
AGGACATGCA TGACACTTCC CAAAGATCCC TCCATAGCGA CACCCTTTCT 3250
GTTTGGACCC ATGGTCATCT CTGTTCTTTT CCCGCCTCCC TAGTTAGCAT 3300
CCAGGCTGGC CAGTGCTGCC CATGAGCAAG CCTAGGTACG AAGAGGGGTG 3350
GTGGGGGGCA GGGCCACTCA ACAGAGAGGA CCAACATCCA GTCCTGCTGA 3400
CTATTTGACC CCCACAACAA TGGGTATCCT TAATAGAGGA GCTGCTTGTT 3450
GTTTGTTGAC AGCTTGGAAA GGGAAGATCT TATGCCTTTT CTTTTCTGTT 3500
TTCTTCTCAG TCTTTTCAGT TTCATCATTT GCACAAACTT GTGAGCATCA 3550
GAGGGCTGAT GGATTCCAAA CCAGGACACT ACCCTGAGAT CTGCACAGTC 3600
AGAAGGACGG CAGGAGTGTC CTGGCTGTGA ATGCCAAAGC CATTCTCCCC 3650
CTCTTTGGGC AGTGCCATGG ATTTCCACTG CTTCTTATGG TGGTTGGTTG 3700
GGTTTTTTGG TTTTGTTTTT TTTTTTTAAG TTTCACTCAC ATAGCCAACT 3750
CTCCCAAAGG GCACACCCCT GGGGCTGAGT CTCCAGGGCC CCCCAACTGT 3800
GGTAGCTCCA GCGATGGTGC TGCCCAGGCC TCTCGGTGCT CCATCTCCGC 3850
CTCCACACTG ACCAAGTGCT GGCCCACCCA GTCCATGCTC CAGGGTCAGG 3900
CGGAGCTGCT GAGTGACAGC TTTCCTCAAA AAGCAGAAGG AGAGTGAGTG ~~4000~~ 3950
CCTTTCCCTC CTAAAGCTGA ATCCCGGCGG AAAGCCTCTG TCCGCCTTTA ~~4050~~ 4000
CAAGGGAGAA GACAACAGAA AGAGGGACAA GAGGGTTCAC ACAGCCCAGT ~~4100~~ 4050
TCCCGTGACG AGGCTCAAAA ACTTGATCAC ATGCTTGAAT GGAGCTGGTG ~~4150~~ 4100
AGATCAACAA CACTACTTCC CTGCCGGAAT GAACTGTCCG TGAATGGTCT ~~4200~~ 4150
CTGTCAAGCG GGCCGTCTCC CTTGGCCCAG AGACGGAGTG TGGGAGTGAT ~~4250~~ 4200
TCCCAACTCC TTTCTGCAGA CGTCTGCCTT GGCATCCTCT TGAATAGGAA ~~4300~~ 4250
GATCGTTCCA CTTTCTACGC AATTGACAAA CCCGGAAGAT CAGATGCAAT ~~4350~~ 4300
TGCTCCCATC AGGGAAGAAC CCTATACTTG GTTTGCTACC CTTAGTATTT ~~4400~~ 4350
ATTACTAACC TCCCTTAAGC AGCAACAGCC TACAAAGAGA TGCTTGGAGC ~~4450~~ 4400
AATCAGAACT TCAGGTGTGA CTCTAGCAAA GCTCATCTTT CTGCCCGGCT ~~4500~~ 4450
ACATCAGCCT TCAAGAATCA GAAGAAAGCC AAGGTGCTGG ACTGTTACTG ~~4550~~ 4500
ACTTGGATCC CAAAGCAAGG AGATCATTTG GAGCTCTTGG GTCAGAGAAA ~~4600~~ 4550
ATGAGAAAGG ACAGAGCCAG CGGCTCCAAC TCCTTTCAGC CACATGCCCC ~~4650~~ 4600
AGGCTCTCGC TGCCCTGTGG ACAGGATGAG GACAGAGGGC ACATGAACAG ~~4700~~ 4650
CTTGCCAGGG ATGGGCAGCC CAACAGCACT TTTCCTCTTC TAGATGGACC ~~4750~~ 4700
CCAGCATTTA AGTGACCTTC TGATCTTGGG AAAACAGCGT CTTCCTTCTT ~~4800~~ 4750
TATCTATAGC AACTCATTGG TGGTAGCCAT CAAGCACTTC GGAATT ~~4846~~ 4796

(2) INFORMATION FOR SEQ ID NO:6
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 924
(B) TYPE: protein
(D) TOPOLOGY: linear
(ii)MOLECULE TYPE: protein
(iii) HYPOTHETICAL: no
(vi) ORIGINAL SOURCE:
(A) ORGANISM: human
(ix) FEATURE: Huntingtin-interacting protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Met Ser Arg Met Trp Gly His Leu Ser Glu Gly Tyr Gly Gln Leu
1 5 10 15

Cys Ser Ile Tyr Leu Lys Leu Leu Arg Thr Lys Met Glu Tyr His
20 25 30

Thr Lys Asn Pro Arg Phe Pro Gly Asn Leu Gln Met Ser Asp Arg
35 40 45

Gln Leu Asp Glu Ala Gly Glu Ser Asp Val Asn Asn Phe Phe Gln
50 55 60

Leu Thr Val Glu Met Phe Asp Tyr Leu Glu Cys Glu Leu Asn Leu
65 70 75

Phe Gln Thr Val Phe Asn Ser Leu Asp Met Ser Arg Ser Val Ser
80 85 90

Val Thr Ala Ala Gly Gln Cys Arg Leu Ala Pro Leu Ile Gln Val
95 100 105

Ile Leu Asp Cys Ser His Leu Tyr Asp Tyr Thr Val Lys Leu Leu
110 115 120

Phe Lys Leu His Ser Cys Leu Pro Ala Asp Thr Leu Gln Gly His
125 130 135

Arg Asp Arg Phe Met Glu Gln Phe Thr Lys Leu Lys Asp Leu Phe
140 145 150

Tyr Arg Ser Ser Asn Leu Gln Tyr Phe Lys Arg Leu Ile Gln Ile
155 160 165

Pro Gln Leu Pro Glu Asn Pro Pro Asn Phe Leu Arg Ala Ser Ala
170 175 180

Leu Ser Glu His Ile Ser Pro Val Val Val Ile Pro Ala Glu Ala
185 190 195

Ser Ser Pro Asp Ser Glu Pro Val Leu Glu Lys Asp Asp Leu Met
200 205 210

Asp Met Asp Ala Ser Gln Gln Asn Leu Phe Asp Asn Lys Phe Asp
215 220 225

Asp Ile Phe Gly Ser Ser Phe Ser Ser Asp Pro Phe Asn Phe Asn
230 235 240

Ser Gln Asn Gly Val Asn Lys Asp Glu Lys Asp His Leu Ile Glu
245 250 255

Arg Leu Tyr Arg Glu Ile Ser Gly Leu Lys Ala Gln Leu Glu Asn
260 265 270

Met Lys Thr Glu Ser Gln Arg Val Val Leu Gln Leu Lys Gly His
275 280 285

Val Ser Glu Leu Glu Ala Asp Leu Ala Glu Gln Gln His Leu Arg
290 295 300

Gln Gln Ala Ala Asp Asp Cys Glu Phe Leu Arg Ala Glu Leu Asp
305 310 315

Glu Leu Arg Arg Gln Arg Glu Asp Thr Glu Lys Ala Gln Arg Ser
320 325 330

Leu Ser Glu Ile Glu Arg Lys Ala Gln Ala Asn Glu Gln Arg Tyr
335 340 345

Ser Lys Leu Lys Glu Lys Tyr Ser Glu Leu Val Gln Asn His Ala
350 355 360

Asp Leu Leu Arg Lys Asn Ala Glu Val Thr Lys Gln Val Ser Met
365 370 375

Ala Arg Gln Ala Gln Val Asp Leu Glu Arg Glu Lys Lys Glu Leu
380 385 390

Glu Asp Ser Leu Glu Arg Ile Ser Asp Gln Gly Gln Arg Lys Thr
395 400 405

Gln Glu Gln Leu Glu Val Leu Glu Ser Leu Lys Gln Glu Leu Gly
410 415 420

Thr Ser Gln Arg Glu Leu Gln Val Leu Gln Gly Ser Leu Glu Thr
425 430 435

Ser Ala Gln Ser Glu Ala Asn Trp Ala Ala Glu Phe Ala Glu Leu
440 445 450

Glu Lys Glu Arg Asp Ser Leu Val Ser Gly Ala Ala His Arg Glu
455 460 465

Glu Glu Leu Ser Ala Leu Arg Lys Glu Leu Gln Asp Thr Gln Leu
470 475 480

Lys Leu Ala Ser Thr Glu Glu Ser Met Cys Gln Leu Ala Lys Asp
485 490 495

Gln Arg Lys Met Leu Leu Val Gly Ser Arg Lys Ala Ala Glu Gln
500 505 510

Val Ile Gln Asp Ala Leu Asn Gln Leu Glu Glu Pro Pro Leu Ile
515 520 525

Ser Cys Ala Gly Ser Ala Asp His Leu Leu Ser Thr Val Thr Ser
530 535 540

Ile Ser Ser Cys Ile Glu Gln Leu Glu Lys Ser Trp Ser Gln Tyr
545 550 555

Leu Ala Cys Pro Glu Asp Ile Ser Gly Leu Leu His Ser Ile Thr
560 565 570

Leu Leu Ala His Leu Thr Ser Asp Ala Ile Ala His Gly Ala Thr
575 580 585

Thr Cys Leu Arg Ala Pro Pro Glu Pro Ala Asp Ser Leu Thr Glu
590 595 600

Ala Cys Lys Gln Tyr Gly Arg Glu Thr Leu Ala Tyr Leu Ala Ser
605 610 615

Leu Glu Glu Glu Gly Ser Leu Glu Asn Ala Asp Ser Thr Ala Met
620 625 630

Arg Asn Cys Leu Ser Lys Ile Lys Ala Ile Gly Glu Glu Leu Leu
635 640 645

Pro Arg Gly Leu Asp Ile Lys Gln Glu Glu Leu Gly Asp Leu Val
650 655 660

Asp Lys Glu Met Ala Ala Thr Ser Ala Ala Ile Glu Thr Cys Thr
665 670 675

Ala Arg Ile Glu Glu Met Leu Ser Lys Ser Arg Ala Gly Asp Thr
680 685 690

Gly Val Lys Leu Glu Val Asn Glu Arg Ile Leu Arg Cys Cys Thr
695 700 705

Ser Leu Met Gln Ala Ile Gln Val Leu Ile Val Ala Ser Lys Asp
710 715 720

Leu Gln Arg Glu Ile Val Glu Ser Gly Arg Gly Thr Ala Ser Pro
725 730 735

Lys Glu Phe Tyr Ala Lys Asn Ser Arg Trp Thr Glu Gly Leu Ile
740 745 750

Ser Ala Ser Lys Ala Val Gly Trp Gly Ala Thr Val Met Val Asp
~~765~~ ~~770~~ ~~775~~
755 760 765

Ala Ala Asp Leu Val Val Gln Gly Arg Gly Lys Phe Glu Glu Leu
~~780~~ ~~785~~ ~~790~~
770 775 780

Met Val Cys Ser His Glu Ile Ala Ala Ser Thr Ala Gln Leu Val
~~795~~ ~~800~~ ~~805~~
785 790 795

Ala Ala Ser Lys Val Lys Ala Asp Lys Asp Ser Pro Asn Leu Ala
~~810~~ ~~815~~ ~~820~~
800 805 810

Gln Leu Gln Gln Ala Ser Arg Gly Val Asn Gln Ala Thr Ala Gly
~~825~~ 815 ~~830~~ 820 ~~835~~ 825
Val Val Ala Ser Thr Ile Ser Gly Lys Ser Gln Ile Glu Glu Thr
~~840~~ 830 ~~845~~ 835 ~~850~~ 840
Asp Asn Met Asp Phe Ser Ser Met Thr Leu Thr Gln Ile Lys Arg
~~855~~ 845 ~~860~~ 850 ~~865~~ 855
Gln Glu Met Asp Ser Gln Val Arg Val Leu Glu Leu Glu Asn Glu
~~870~~ 860 ~~875~~ 865 ~~880~~ 870
Leu Gln Lys Glu Arg Gln Lys Leu Gly Glu Leu Arg Lys Lys His
~~885~~ 875 ~~890~~ 880 ~~895~~ 885
Tyr Glu Leu Ala Gly Val Ala Glu Gly Trp Glu Glu Gly Thr Glu
~~900~~ 890 ~~905~~ 895 ~~910~~ 900
Ala Ser Pro Pro Thr Leu Gln Glu Val Val Thr Glu Lys Glu
~~915~~ 905 ~~920~~ 910 ~~924~~ 914